UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,766	12/29/2006	Hideki Hasegawa	43512-103808	5560

23643 7590 12/23/2011

BARNES & THORNBURG LLP
11 SOUTH MERIDIAN
INDIANAPOLIS, IN 46204

EXAMINER	
KINSEY WHITE, NICOLE ERIN	
ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
12/23/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

indocket@btlaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/567,766	HASEGAWA ET AL.	
	Examiner	Art Unit	
	NICOLE KINSEY WHITE	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *11-14 and 23-34* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *11-14 and 23-34* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/26/2011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Nicole Kinsey White, Group Art Unit 1648.

Withdrawn Rejections

The rejection of claims 11-14 under 35 U.S.C. 103(a) as being unpatentable over Moldoveanu et al. (Vaccine, 1998, Vol. 16, p. 1216-1224) in view of Wong et al. (Antimicrobial Agents and Chemotherapy, 1995, Vol. 39, p. 2574-2576) has been withdrawn in view of applicant's arguments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11-14 and 23-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moldoveanu et al. (Vaccine, 1998, Vol. 16, p. 1216-1224) in view of Singh et al. (The Journal of Infectious Diseases, 1970, 122(4):339-342) and Samuel (Clin. Microbiol. Rev., 2001, 14(4):778-809).

The claims are directed to a method of preventing influenza, comprising a step of administering to nasal mucosa at least once: a vaccine at a concentration sufficient to produce secretory IgA, wherein said vaccine comprises:

a) an isolated double-stranded RNA;

b) a subunit antigen or inactivated antigen of an influenza virus; and

c) a pharmaceutically acceptable carrier, wherein said carrier is selected from the group consisting of water, an aqueous physiological solution, and an artificial aqueous cerebrospinal fluid.

The claims are interpreted as being directed to preventing influenza disease and symptoms of influenza infection.

Moldoveanu et al. teaches a method for preventing influenza infection comprising administering influenza HA protein and CpG DNA in an aqueous solution to the nasal mucosa in mice (see page 1217 under Immunization and page 1220 right column and Figure 4). Moldoveanu teaches generation of secretory IgA antibody responses in mice immunized intranasally with influenza HA protein and CpG DNA in an aqueous solution (see Figure 4 and Discussion).

Moldoveanu et al. also teaches that the immune effects of DNA containing CpG motifs (CpG DNA) include: induction of B cell proliferation and differentiation; induction of monocyte secretion of IL-12 and other cytokines; and the subsequent activation of natural killer (NK) cell interferon-γ (IFN-γ) secretion and lytic activity.

Moldoveanu does not teach administering double stranded RNA such as Poly(I:C).

Singh et al. teaches that the double-stranded complex consisting of polyriboinosinic and polyribocytidylic acids (poly I:C) has been shown to be a potent inducer of interferon and effective prophylactically against a number of experimental viral infections. Poly I:C can stimulate the appearance of antibody-forming cells and potentiate the antibody response to influenza viral vaccine in adjuvant 65 (see Introduction). Regarding Japanese B Encephalitis (JBE) virus, Singh et al. found that "[e]nhanced protection following administration of poly I:C and vaccine correlated with a 4-fold rise in the titer of neutralizing antibody at the time of challenge. . . . Taken together, these data are in general agreement with those of Woodhour et al. with the following exceptions: the potentiation of the antibody response to JBE virus was clearly demonstrable by injection of the vaccine and poly I:C by different routes. . . ." Singh et al. used poly(I:C) at the concentration of 0.5 mg/ml.

Thus, CpG and poly(I:C) are taught as inducers of interferon. Interferon is known in the art as having potent antiviral effects (see, for example, Samuel). Further, CpG activates Toll-like Receptor 9 (TLR9), which leads to the production of interferon and inflammatory cytokines, and dsRNA activates Toll-like Receptor 9 (TLR3), which leads to the production of interferon (see applicant's exhibits dated September 12, 2011).

It would have been obvious to one of ordinary skill in the art to modify the methods taught by Moldoveanu et al. and add poly(I:C) to the vaccine as another agent to produce interferon and enhance antibody production. One would have been motivated to do so given the teachings in the art that interferon is a potent antiviral and given the teachings that poly(I:C) and CpG induce interferon by different pathways.

Thus, by administering poly(I:C) and CpG one of ordinary skill in the art would ensure the production of interferon via two distinct pathways. In addition, one of ordinary skill in the art would be motivated to add poly(I:C) to benefit from its prophylactic and antibody inducing effects. There would have been a reasonable expectation of success given the teachings and findings of the cited references.

The claims are directed to at least one administration of the vaccine (claim 11) and up to at least two administrations of the vaccine (12-13 and 30). Moldoveanu et al. teaches at least one administration of the vaccine that resulted in the production of secretory IgA. Therefore, determining other dosing schedules that result in the production of secretory IgA is routine experimentation (e.g., adding booster administrations). Further, applicant has not demonstrated unexpected results for the claimed dosing schedules.

Regarding claims 26, 27 and 34, the length of dsRNA (poly(I:C)) administered by Moldoveanu et al. was sufficient to produce secretory IgA. Therefore, determining additional lengths of dsRNA (poly(I:C)) that also produce secretory IgG is routine experimentation. It is obvious and routine to determine additional amounts of an agent to be administered to achieve a desired effect. Further, applicant has not demonstrated unexpected results for the claimed amounts and lengths of dsRNA.

Furthermore, according to section 2144.05 of the MPEP, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. “[W]here the general conditions of a claim are disclosed in the

prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.") As outlined above, Knopf et al. teaches the general conditions of the claim.

Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 11-14 and 23-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knopf et al. (Vaccine, 1998, Vol. 16, p. 1216-1224) in view of Zahradnik et al. (Journal of Medical Virology, 1983, 11:277-285), Waldman et al. (The Journal of Immunology, 1973, 111(1):38-41), Barackman et al. (Infection and Immunity, 1999, 67(8):4276-4279) and Chen et al. (Journal of General Virology, 1999, 80:2559-2564).

Knopf et al. teaches the intranasal administration of influenza with poly(I:C). Knopf et al. states that "[i]n previous experiments, we observed that the simultaneous intranasal administration of inactivated rhinovirus or influenza virus with poly I:C produced a definite enhancement of serum antibody and a relative increase in local production of antibody (nasal secretory type) to these viruses. In addition, we noted an incidental rise in tear antibody to these organisms, similar to our previous experiments

in human volunteers." Knopf et al. goes on to state that "[t]he nasal submucosa and lacrimal gland stroma contain plasma cells which produce mainly IgA. It follows that intranasal administration of an antigen will stimulate primarily IgA production in nasal cells. In addition, it will enhance tear IgA by either direct or indirect transfer of antigen or cells." See page 757. The production of IgA nasal secretory type antibodies is known in the art to result from intranasal influenza immunizations (see, for example, Zahradnik et al. and Waldman et al.).

Knopf et al. does not specifically teach a pharmaceutically acceptable carrier. However, the use of a carrier such as water or an aqueous physiological solutions to administer an influenza vaccine intranasally is routine and obvious in the vaccine arts (see, for example, Barackman et al., which teaches intranasal administration of an influenza vaccine in phosphate-buffered saline).

Knopf et al. also does not teach a subunit antigen (Knopf et al. used the entire virus). Given the teachings and findings of the prior art regarding influenza vaccines, it would be obvious for one of ordinary skill in the art to administer either influenza proteins such as hemagglutinin or neuraminidase or the entire virus (see, for example, Zahradnik et al., Waldman et al. and Chen et al.).

The claims are directed to at least one administration of the vaccine (claim 11) and up to at least two administrations of the vaccine (12-13 and 30). Knopf et al. teaches at least one administration of the vaccine that resulted in the production of secretory IgA. Therefore, determining other dosing schedules that result in the production of secretory IgA is routine experimentation (e.g., adding booster

administrations). Further, applicant has not demonstrated unexpected results for the claimed dosing schedules.

Regarding claims 24-27, 33 and 34, the amount and length of dsRNA (poly(I:C)) administered by Knopf et al. was sufficient to produce secretory IgA. Therefore, determining additional amounts or lengths of dsRNA (poly(I:C)) that induce secretory IgA is routine experimentation. It is obvious and routine to determine additional amounts of an agent to be administered to achieve a desired effect. Further, applicant has not demonstrated unexpected results for the claimed amounts and lengths of dsRNA.

Furthermore, according to section 2144.05 of the MPEP, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.") As outlined above, Knopf et al. teaches the general conditions of the claim.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 11-14 and 23-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6-12 of copending Application No. 13/262,515.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they relate to the same inventive concept. Both sets of claims are directed to a method of preventing influenza, comprising a step of administering a vaccine composition comprising an effective amount of an influenza virus antigen and poly (I:C) at least once to the nasal mucosa of a subject in need thereof.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NICOLE KINSEY WHITE whose telephone number is (571)272-9943. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on (571) 272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nicole Kinsey White/
Examiner, Art Unit 1648

/Stacy B. Chen/
Primary Examiner, Art Unit 1648